

## **REMARKS**

### **Finality of Rejection**

At the outset, Applicants respectfully question the propriety of making this Office Action final. It is based on entirely new rejections that were not previously made, and that were not necessitated by Applicants' amendments to the claims. In particular, Applicants' object to the new obviousness rejection based on Johnson et al. (1999) over Bolon (1999), and respectfully request that the finality of the office action be withdrawn.

### **Objections to the Specification**

The Office Action objects to the alleged presence of embedded hyperlinks in the text of the application on page 26. In response, the Applicants have deleted the objectionable text from the specification.

### **Claim Rejections – 35 U.S.C. § 112**

The Office Action rejects claims 1 and 19 because they recite a method for improving the binding affinity of a ligand for a target and do not provide a step of improving the binding affinity. While the applicants do not believe that such a step is required in the claim, inasmuch as the step necessarily occurs when one carries out the recited sequence of steps, out of a spirit of cooperation and in order to have the application more promptly issued to allowance, applicants have amended claims 1 and 19 to indicate that the binding affinity of the first ligand for the biological target is improved by the process.

The Office Action also rejects claims 20 because it uses the term "substantially." The Office Action states that the term does not adequately express the metes and bounds of the claim. Applicants respectfully submit that a skilled worker would know precisely what is meant by the term "substantially," based on inherent limitations in the process of constructing composite ligands, and inherent limitations on the detection equipment that is employed when practicing the claimed invention. The term "substantially" simply allows for that level of variability within these and other processing conditions that are known to all skilled workers.

The applicants take issue with the Patent Office's suggestion that "substantially" should be numerically expressed, such as by reciting the distance between the two ligands when joined

together. The Patent Office appears to be suggesting that applicants impose additional limitations on its invention that are not commensurate with the scope of their invention. Breadth and definiteness are two distinct concepts under the patent laws. It is respectfully submitted that a skilled worker would not consider the metes and bounds of the claim indefinite based upon the presence of the term “substantially.”

### **Claim Rejections – 35 U.S.C. § 103**

The Office Action also states a new ground of rejection for alleged obviousness under 35 U.S.C. § 103 over Johnson et al. (1999) in view of Bolon et al. (1999). Applicants respectfully submit that these references do not support a prima facie case of obviousness because they do not disclose the use of NMR spectroscopy to construct composite ligands from first and second ligands, as recited in the pending claims. They also do not suggest the construction of such composite ligands.

Johnson et al. is a paper co-authored in 1999 by Dr. Jim Prestegard -- an inventor on this application. The paper discloses the results of work to characterize the domain orientation of two domain fragment of barley lectin. Johnson et al. did not bind two ligands to the lectin, and did not determine the relative distance and orientation of two ligands when bound to the protein, to construct a composite ligand with enhanced binding affinity for the biological target, as recited in the pending claims. Johnson was focused on the structure of the protein – not the structure of the ligand for the protein – and would not have motivated a skilled worker to construct the composite ligands of the present invention.

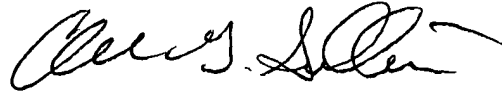
The newly cited Bolon (1999) reference does not cure this deficiency. This article was also co-authored by Dr. Prestegard. Bolon (1999) report the determination of a ligand's average orientation when bound to a biological target based upon observations of residual dipolar couplings. The article only analyzed the orientation of a single ligand relative to a protein structure. The authors did not bind two different ligands to the protein structure, deduce the relative orientations of the ligands, or determine the distance between the ligands, in order to improve the binding affinity of a ligand for the biological target. In short, the reference did not offer any suggestion or motivation for constructing composite ligands based upon their relative distances and orientations when bound to a protein, as recited in the pending claim. Lacking

such a suggestion or other motivation, the references do not support a prima facie case of obviousness.

**CONCLUSION**

Please grant any extension of time required to enter this response and charge any additional fee, or credit any overpayment to Deposit Account No. 11-0980.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Clark G. Sullivan", with a stylized flourish at the end.

Clark G. Sullivan  
Reg. No. 36,942

December 27, 2004  
KING & SPALDING LLP  
191 Peachtree Street  
Atlanta, GA 30303  
(404) 572-4600 (Telephone)  
(404) 572-5145 (Facsimile)  
04342.105053